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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,307	10/14/2003	Martin Bluggel	B0004/7115	9843

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EXAMINER	
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ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/685,307	BLUGGEL ET AL.	
	Examiner	Art Unit	
	PAUL S. HYUN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12 remain pending. Applicant amended claim 1. Despite the amendment, the art rejections are maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims **1-3, 7 and 8** are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (US 2002/0139751 A1).

Zhang et al. disclose an electrospray device comprising a capillary column and a microchip array arranged in a series (see Figs. 5-8). The device can be coupled to a mass spectrometer (see [0013]) to identify proteins (see [0048]). The device can be used to conduct two-dimensional chromatography if the capillary column and the microchip array comprise different affinity adsorbents therein (see [0072]). In one embodiment, the capillary column is packed with a porous polymer monolith, and the channels of the microchip array are packed with a different porous polymer monolith that is covalently bound to the surfaces of the channels via alkyl groups. The capillary column serves as an ion-exchange column that separates a sample mixture into fractions based on charge, and the microchip array serves as hydrophobic adsorption columns separating the fraction into sub-fractions. Alternatively, instead of using porous polymer monoliths, the two-dimensional chromatography can be formed using two different types of affinity ligands (see [0071]). The sub-fractions can be further

processed (e.g. proteolysis digestion using an endoprotease) prior to analyzing the sub-fractions with the mass spectrometer (see [0070]).

Claims **1-3, 5, 6, 8, 11 and 12** are rejected under 35 U.S.C. 102(b) as being anticipated by LaDine et al. (US 2002/0068366 A1).

LaDine et al. disclose a method for conducting two-dimensional chromatography to separate a mixture of peptides (see [0039]). The two-dimensional chromatography can be carried out using microplates wherein the wells of the microplates are loaded with magnetic particles derivatized with functional groups configured to bind various analytes of interest. A first microplate wherein each well of the microplate contains a unique type of functionalized particles is used to separate the sample into fractions (see [0092]-[0114]). The fractions are then further separated into sub-fractions using a second microplate. The sub-fractions can be further processed (e.g. digestion (see [0038])) before they are transferred to a MALDI plate and analyzed using mass spectrometry (see [0056]). The sample can be fractionated based on affinity, hydrophobicity and charge (see [0110]). The reference discloses that the procedural steps for conducting the two-dimensional chromatography can be facilitated by using a robotic pipette (see [0029]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims **4 and 7** are rejected under 35 U.S.C. 103(a) as being unpatentable over LaDine et al. in view of Hammen (US 5,240,602).

LaDine et al. do not disclose the step of coating the inner surface of the wells of the microplates with substance-binding layers. Rather, LaDine et al. disclose the use of functionalized magnetic particles disposed in the wells to bind the analyte of interest.

Hammen discloses a method for conducting affinity chromatography to isolate at least one substance, such as protein, from a mixture of substances (see lines 12-40, col. 6). The method comprises the step of affixing affinity ligands to the wells of a microtiter plate, incubating the sample mixture with the ligands, and washing the ligands to remove the unbound species. In light of the disclosure of Hammen, it would have been obvious to one of ordinary skill in the art to utilize immobilized ligands to bind the analyte of interest instead of using functionalized magnetic particles. Immobilized ligands would be easier to process (i.e. wash) than particles that are suspended in the wells.

Claims **9 and 10** are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. in view of Cortes et al. (US 5,240,604).

Zhang et al. disclose different types of liquid chromatography (e.g. ion-exchange, affinity) to separate a sample mixture, but the reference does not disclose the use of size exclusion chromatography.

Cortes et al. disclose a multidimensional chromatographic system wherein the first separation phase is size-exclusion chromatography conducted in a micro column (see lines 39-65, col. 3). Using this method, the sample can be first separated according to size. In light of the disclosure of Cortes et al., it would have been obvious to incorporate a size-exclusion chromatography column into the device disclosed by Zhang et al. so that the protein mixture can be separated according to size.

Response to Arguments

Applicant's arguments with respect to the Zhang et al. reference have been fully considered but they are not persuasive:

1) Applicant argues that Zhang et al. do not disclose the step of further processing or analyzing each sub-fraction. Specifically, Applicant argues that the reference is silent with regards to whether all the sub-fractions are further processed or analyzed. This argument is not persuasive because the claims do not recite that each sub-fraction must be further processed or analyzed. Claim 1 is only directed to a method of producing sub-fractions. Claim 1 does not recite a step of further processing or analyzing each sub-fraction. The preamble of the claim even specifies that the claimed invention is directed towards separating the sample PRIOR to subjecting the sample to a mass spectrometer. That said, a reference only needs to disclose a method of separating a sample into sub-fractions to anticipate claim 1. Therefore, Applicant's

argument that Zhang et al. do not anticipate the claimed invention because the reference is silent with regards to whether all the sub-fractions are further processed or analyzed is not persuasive.

2) Applicant argues that the method disclosed by Zhang et al. produces only one sub-fraction, and not a plurality of sub-fractions as recited in the claims. This argument is not persuasive because the method disclosed by Zhang et al. must inherently produce at least two sub-fractions. The term "sub-fraction" means a fraction of a fraction. In other words, the term "sub-fraction' indicates that the fraction has been further divided into even smaller fractions. Therefore, by definition, any method that separates a fraction must produce at least two sub-fractions. In this instance, Applicant acknowledges that the method disclosed by Zhang et al. includes the step of separating a fraction. Specifically, Applicant acknowledges that the fraction is introduced into a chip array that contains adsorbents that bind analytes. Thus, the method disclosed by Zhang et al. does produce at least two sub-fractions (i.e. one sub-fraction that binds the adsorbents and another sub-fraction that doesn't bind the adsorbents). It appears that the basis of Applicant's argument is dependent on whether the sub-fractions are further processed and analyzed. As, indicated above, the claimed invention is only directed towards a method of PRODUCING sub-fractions. Thus, whether Zhang et al. disclose the step of further processing the sub-fractions is irrelevant.

3) Applicant also argues that not all of the biosubstances in the fraction disclosed by Zhang et al. is further separated because the fraction is divided into aliquots prior to subjecting the fraction to the second phase of separation. This argument is not

persuasive because the fraction is divided based on volume, not content. Thus, the composition of one aliquot is identical to the other aliquots. Moreover, because each aliquot is subjected to a second phase of separation (i.e. none of the aliquots are discarded), all of the biosubstances present in the initial sample are subjected to two phases of separation.

4) Applicant argues that the separation method disclosed by Zhang et al. does not employ a series of separations because the method divides the sample into aliquots. This argument is not persuasive because the separation method disclosed by Zhang et al. does employ a series of separations. The fact that a method employs parallel processing (i.e. divides the sample into aliquots) does not preclude it from also employing series processing because parallel processing and series processing are not mutually exclusive. In the context sample separation, a separation is deemed to be employing series processing if it involves two phases of separation. The method disclosed by Zhang et al. meets this requirement.

Applicant's argument with respect to the LaDine et al. reference has been fully considered but it is not persuasive:

1) Applicant argues that LaDine et al. disclose parallel processing of samples, and therefore the reference does not anticipate the claims. This argument is not persuasive. As explained above, parallel processing and series processing are not mutually exclusive. Although LaDine et al. employs parallel processing because it initially splits the sample into aliquots, each aliquot is subjected to 2 phases of separation. Thus, each aliquot is subjected to series processing. Moreover, because all

the aliquots are subjected to two phases of separation, all the biosubstances in the initial sample is processed in a series manner.

With respect to the dependent claims, because Zhang et al. and LaDine et al. disclose all the limitations recited in claim 1, Applicant's arguments with respect to the dependent claims are moot. For the foregoing reasons, the rejections are maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL S. HYUN whose telephone number is (571)272-8559. The examiner can normally be reached on Monday-Friday 8AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Paul S Hyun/
Examiner, Art Unit 1797

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797